REMARKS

In the instant Office Action, a restriction of Applicants' invention was required as between:

> I. Claims 1-9, drawn to peptides, classified in class 530, subclass 324, and their pharmaceutical composition classified in class 514, subclass 12;
> II. Claim 10, drawn to eliciting an agonist effect from a GLP-1 receptor, classified in class 514, subclass 12; and
> III. Claims 11-12, drawn to a method of treating various diseases using product of Group I, classified in class 514, subclass 12.

The Examiner further sub-divides Group III claims into 16 sub-groups, each directed to a method of treating one of the indications recited in claim 11.

Applicants respectfully traverse this requirement and request consideration of all claims together in this application for the reasons set forth below.

In support of the restriction requirement, the Examiner alleges that separate inventions exist because

> [t]he inventions listed as Groups I - III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Group I is the technical feature that links Groups I to III. Group II is not the contribution over the prior art because it is described or suggested by references teaching GLP-1 derivatives encompassed by the instant claims; see, for example, Buckley et al. (US Patent 5,545,618) teaching homologous derivatives. Therefore, the lack of unity is present because the linking technical feature is not a "special technical feature" as defined by PCT Rule 13.2.

Applicants note that PCT Rule 13.1 requires that an application "shall relate to one invention only or to a group of inventions so linked as to form a general inventive concept." PCT Rule 13.2 states that the unity of invention of Rule 13.1 "shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features." The text continues by stating that "the expression 'special technical features' shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art."

In light of these PCT Rules, Applicants respectfully submit that the Examiner has misunderstood the claimed invention. The Examiner notes on page 4 that "Group II is not the contribution over the prior art because it is described or suggested by references teaching GLP-1 derivatives encompassed by the instant claims; see, for example, Buckley et al. (US Patent 5,545,618) teaching homologous derivatives." Applicants respectfully point out that the sole claim of Group II (claim 10) is drawn to a method of eliciting an agonist effect from a GLP-1 receptor. Applicants respectfully submit that the "special technical feature" of the claims of Group I, namely the novel compounds of formula I, are a contribution over the prior art and are the special technical feature which unifies

Group I and claims 10-12, which depend, either directly or indirectly, from the novel compounds of claim 1.

On page 4, the Examiner states that "Inventions I and II, III [sic] are related as product and processes of use. Methods II, III.1-III.16 are alternate methods of using the compound of Group I; the product as claimed can be used in a materially different processes [sic] such as peptide synthesis; the methods of use can be practiced with a broad variety of drugs beyond the claimed peptides." Applicants respectfully point out that most, if not all, products can be used in more than one manner and that such a vague and sweeping application is beyond the spirit and scope of 35 U.S.C. § 121. Applicants further note that if such an interpretation is used, then product and process of use claims can never be considered together because every product can be used in some type of alternative method.

Further on page 4, the Examiner also states that "inventions II and III are related as different methods which are not connected in design, operation or effect. The methods have different functions and different effects, and a reference teaching treatment of e.g., heart failure, will not necessarily teach eliciting agonist effect from GLP receptors." Applicants respectfully submit that the methods of Groups II and III are related as they utilize the compound of Group I. Applicants also submit that the Examiner has not provided a basis in the art or in Applicants' disclosure indicating that the function of

eliciting an agonist effect from GLP receptors is necessarily a different function and/or a different effect that is separate from the treatment of a condition.

The Examiner continues on page 4 to page 5 by noting that "the methods of use III.1 - III.16 are drawn to methods of treatment of 16 distinct disorder conditions which are patentably distinct because the disorder conditions are not related to each other, have different mechanisms, development and etiology, and the methods of treatment have different enablement requirements. The groups require different literature search [sic] and a reference teaching treatment of one disorder . . . will not teach treatment of any other disorder . . . "

Applicants respectfully submit that simply because the listed conditions have different mechanisms, developments or etiologies[1] does not make it true that a single compound, e.g. a GLP-1 analogue of the instant invention, cannot affect more than one parameter or more than one condition, or that information on different conditions cannot be found together in a given reference. Applicants also submit that the Examiner has not provided any evidence that the conditions of Group III.1 to III.16 are exclusive or necessarily unrelated, and that having one of the listed conditions, such as arthritis, necessarily excludes having another one of the listed conditions, such as hypertension,

and as such would never be reported together in the literature. In fact, Applicant has found several references indicating that a patient may have more than one of the conditions recited in claims 11 and 12. For example, a patient with diabetes may well also be obese (see attached abstract Exhibit A: Rendel, Med. Gen. Med., 2004, Sep 6(2):10) or a patient with nephrotic syndrome may well suffer from renal failure (see attached abstract Exhibit B: Agarwal, Pediatr. Nephrol., 2003, 18(12):1289-92).

Applicants submit that the Examiner has not shown that the listed conditions are so unrelated that treatment with a GLP-1 analogue of a claim of Group I would not have an effect on more than one condition claimed by the Applicants or that it is even possible to treat one condition with a single compound, e.g. an analog of GLP-1, and not be able to affect and/or treat other conditions in the body.

Applicants also note, further, that the Examiner has classified groups II and III as well as part of group I, falling within not only the same class (514), but the same subclass as well (12). The fact that groups I, II and III share the same class and subclass strongly mitigates against the conclusion that the demarcated inventions do not form a single inventive concept. Applicants remind the Examiner MPEP §803, paragraph 2, which states:

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[1] The Examiner's opinion that the recited conditions have different methods of treatment is incorrect since the claimed method of treatment, i.e. administration of a compound of formula (I), for each recited condition.

> If the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to independent or distinct inventions.

(emphasis added). MPEP §803 goes on to state, at approximately the fourth paragraph following the subheading GUIDELINES:

> For purposes of the initial requirement, a serious burden on the examiner may be *prima facie* shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search as defined in MPEP §808.02.

Applicants respectfully submit that the Examiner has failed to establish a *prima facie* showing that a serious burden will arise. To wit, the Examiner has shown neither a separate classification, nor a separate status in the art, nor still a different field of search, as defined in MPEP §808.02. In addition, Applicants respectfully state that no serious burden will arise from examining group I concurrently with groups II and III since any search performed in respect of group I necessarily must contemplate the subject matter of groups II and III. Conversely, any search performed in respect of group I manifestly would involve significant overlap with a search performed in respect of groups II, III and IV. Surely such a search would will reveal not only art pertinent to the GLP-1 analogues, (group I), but use thereof (groups II and III). As such the Examiner's allegation that "[t]he groups require different literature search [sic]" is unfounded.

Conclusion and Provisional Election:

Applicants respectfully submit that in view of the foregoing remarks, all of the claims herein are seen to relate to a single inventive concept, a compound of formula (I) and use thereof, and that the claims are in a form and are of the sort that is properly viewed as relating to a single invention that should not be restricted. Applicants respectfully request that the restriction requirement of the Office Action of February 9, 2005 be reconsidered and withdrawn.

Although, for reasons set forth above, Applicants believe that the restriction is improper, and without in any way acquiescing in the reasons for the requirements set forth in the Office Action, but in order to be fully responsive to the Office Action, Applicants provisionally elect for examination of the claims of **Group I, *i.e.*, drawn to peptides, classified in class 530, subclass 324, and their pharmaceutical composition classified in class 514, subclass 12 and withdraw claims 10-12**. Applicants state that withdrawal of the unelected subject matter does not require any amendment of inventorship pursuant to 37 C.F.R. 1.48(b).

Applicants reserve the right to pursue any withdrawn subject matter in future applications.

As per the request of the Examiner on page 6-7, under "Species Requirement," Applicants provisionally elect the compound **[Hppa^7]hGLP-1(7-36)-NH_2**.

Also as per the request of the Examiner, Applicants note that the selected species reads upon Claims 1-7 and 9.

Request for Rejoinder:

Applicants note that method claims 10 - 12 are subject to rejoinder upon the allowance of product claims 1-9. As noted by the Examiner and in the MPEP821.04:

> [I]f Applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims which depend from or otherwise include all the limitations of the allowable product claim will be rejoined . . . Process claims which depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment if presented prior to final rejection or allowance.

Applicants submit that claims 10-11 currently incorporate the limitation of claim 1 by the language "a compound according to claim 1." In a similar manner, claim 12 currently incorporates the limitation of claim 1 by the language "according to claim 11" wherein claim 11 incorporates the compound according to claim 1, therefore, Group II and Group III claims would be appropriate for rejoinder upon allowance of Group I product claims 1-9.

Reconsideration of the instant Office Action and allowance of all pending claims are respectfully requested. Prompt and favorable action is solicited.

Should Examiner Borin deem that any further action by the Applicants would put this application in order for acceptance, he is requested to contact the Applicants' undersigned representative.

The Commissioner is hereby authorized to charge any additional fees associated with this communication or credit any overpayment to Deposit Account No. 50-0590.

Respectfully submitted,

Date:
6/8/2005

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1: MedGenMed. 2004 Sep 01;6(2):10.

Advances in diabetes for the millennium: nutritional therapy of type 2 diabetes.

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Dietary modification is useful in both type 1 and type 2 diabetes. Glucose levels after a meal are largely determined by carbohydrate intake. Decreased intake of simple carbohydrates and increased fiber consumption lower postprandial glucose.Obesity has become epidemic in the United States and has dramatically increased the incidence of type 2 diabetes by augmenting insulin resistance. Dietary treatment of obesity has been frustrating. Success will require education in using foods with high fiber contents, low glycemic indexes, and low saturated fat levels. The use of natural foods must be supplemented by the use of semisynthetic foods with desirable properties. The educational efforts required are substantial and must be recognized by third-party reimbursement agencies. Operative procedures to decrease intake or reduce the absorption of food are being used with increasing frequency. Bariatric surgery is often successful in inducing a substantial loss of weight; however, this success must be balanced against the complications of surgery, which can be considerable.The pharmacologic approaches to treatment of obesity have focused primarily on anorexigenic agents. Several polypeptides that induce satiety are currently under study, including leptin and glucagon-like peptide-1 (GLP-1). Orlistat has been used to induce the malabsorption of fat to reduce caloric ingestion. Of the currently used oral hypoglycemics, metformin and the disaccharidase inhibitors have the best tendency to promote weight loss. There is active research on the uncoupling proteins that induce thermogenesis and promote the dissipation of calories. The beta-3 agonists act through the uncoupling proteins. The thiazolidinediones tend to promote weight gain through the PPAR gene locus. Agents that antagonize this effect could induce weight loss. The future will undoubtedly bring us drugs that are effective in causing weight loss. The advent of drugs to successfully combat obesity will substantially improve public health.

PMID: 15647715 [PubMed - in process]

EXHIBIT "A"

1: Pediatr Nephrol. 2003 Dec;18(12):1289-92. Epub 2003 Oct 24.

Acute renal failure in children with idiopathic nephrotic syndrome.

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Acute renal failure (ARF) is an uncommon but alarming complication of idiopathic nephrotic syndrome. The renal failure could be secondary to causes evident from the history and evaluation, such as severe intravascular volume depletion, acute tubular necrosis, allergic interstitial nephritis, bilateral renal vein thrombosis, acute pyelonephritis, or rapid progression of the original glomerular disease. It may be termed idiopathic if the underlying cause is undetermined. We present three children with idiopathic nephrotic syndrome who were admitted with acute renal failure. One case was due to drug-induced allergic interstitial nephritis. The other two were idiopathic in nature. Improvement in renal function occurred in the three patients over a variable period of 10 days to 4 weeks. After careful exclusion of well-known causes of acute renal failure, idiopathic acute renal failure (IARF) should be considered as a diagnostic possibility in these patients. The exact pathophysiology of IARF is not understood. Possible proposed explanations include interstitial edema, tubular obstruction, altered glomerular permeability, and unrecognized hypovolemia.

Publication Types:
Case Reports

PMID: 14579139 [PubMed - indexed for MEDLINE]

EXHIBIT "B"